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Simulation of the Spontaneous Aggregation of Phospholipids into Bilayers

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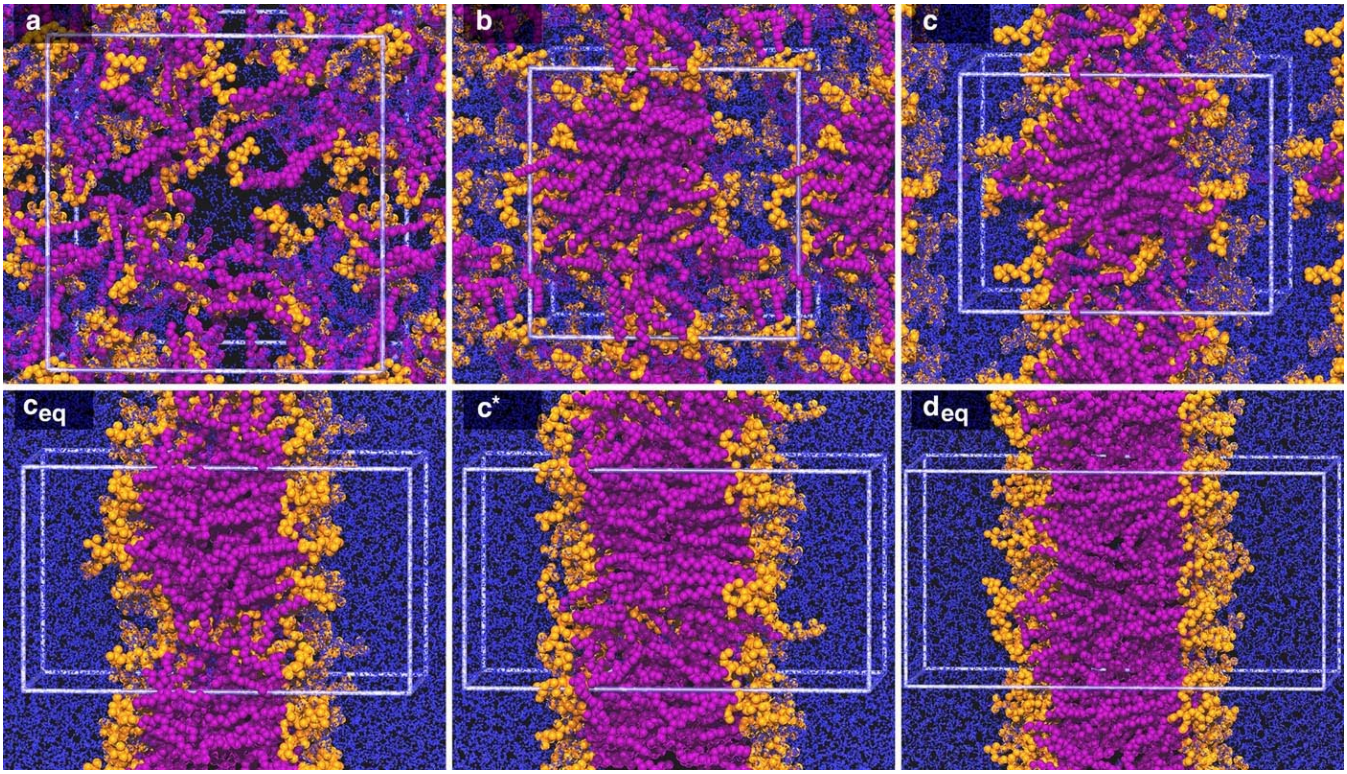
SUPPORTING INFORMATION FOR THE COMMUNICATION



Supporting figure S1 Snapshots of the phospholipids assembling into a bilayer. Headgroup atoms are depicted with orange spheres, while tail atoms are purple and water molecules drawn small in blue. For clarity, the system is repeated in space and the actual simulation box shown as a light blue frame. Starting from the random solution (**a**), large thermodynamic gradients drive an aggregation into irregular clusters at 200 ps (**b**). This is followed by the formation of a primordial bilayer shown at 3 ns (**c**) and subsequent relaxation towards a metastable structure with a transmembrane pore reached after 10 ns ($\mathbf{c}_{eq}$). This water pore is relatively stable and involves a significant free energy barrier, but once the disruption starts and the transition state is reached at about 20 ns ($\mathbf{c}^{*}$) the defect disappears very rapidly and the system reaches an equilibrated perfect bilayer configuration after a total 25 ns ($\mathbf{d}_{eq}$). The properties of the final system match both other simulations and experimental data.

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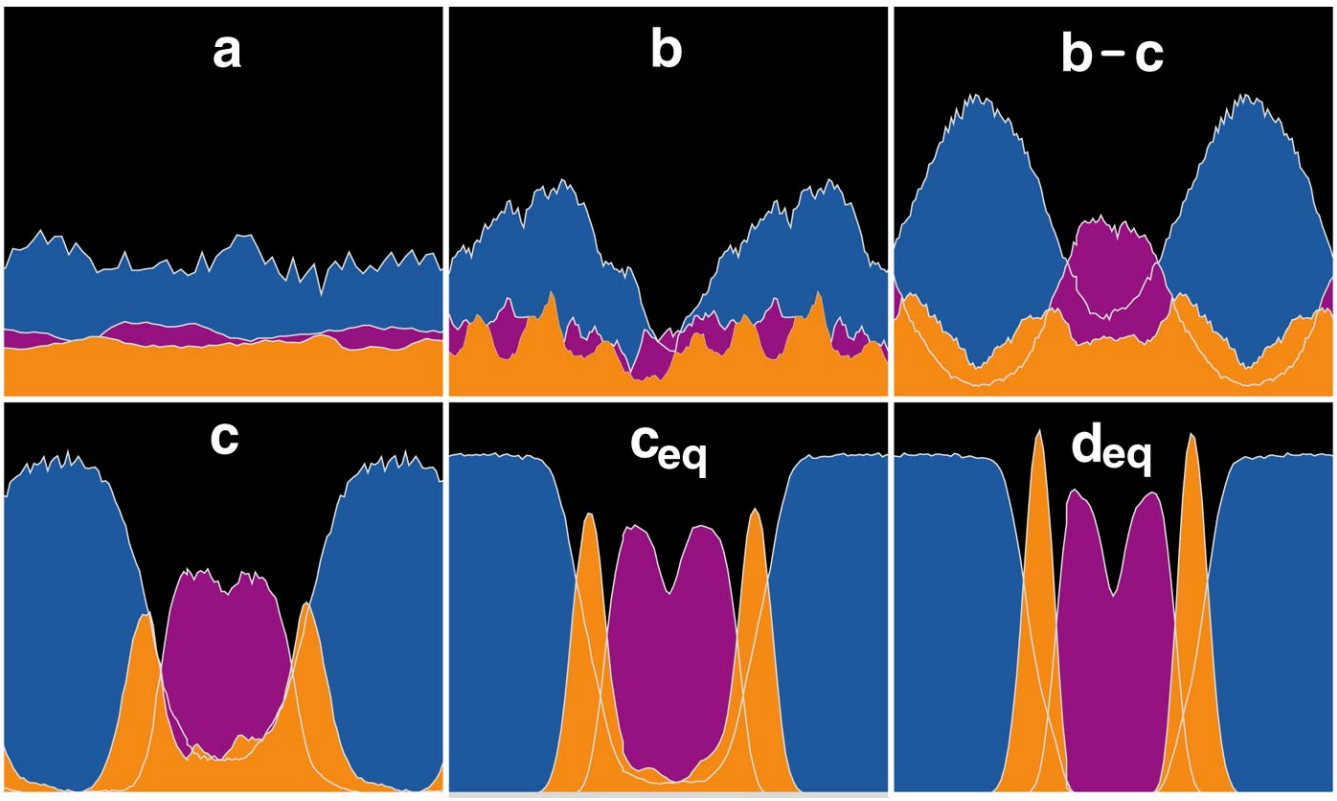
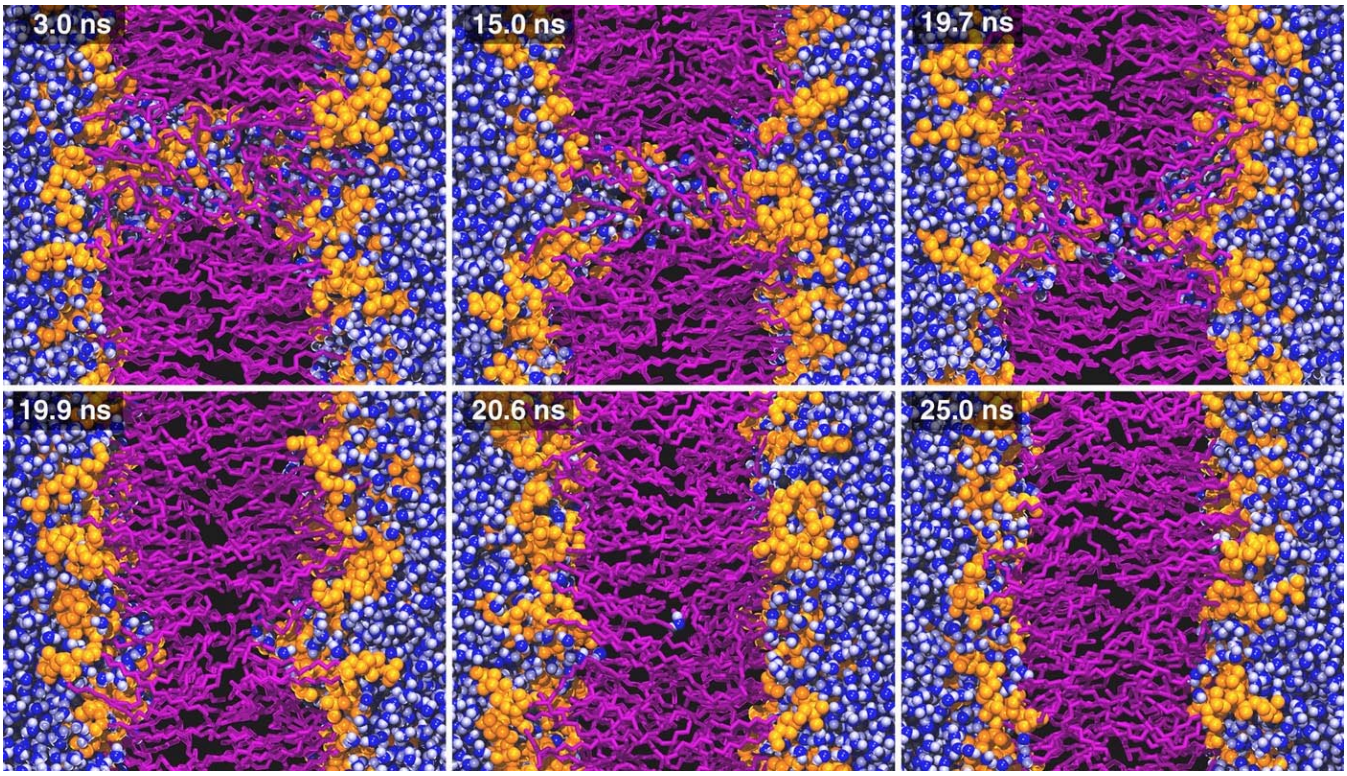


Supporting figure S2 Atom number density distributions during the bilayer self-assembly process, resolved along the eventual membrane normal. Orange indicates lipid headgroups, purple tails, and blue water molecules. The densities are calculated as averages over six different parts of the trajectory, with labels corresponding to the stages in Fig. S1 above (and Fig. 1 in the paper): The initial random solution of lipids (**a**), aggregation into irregular clusters in the interval 100-500ps (**b**), clusters gradually becoming more regular with clear lateral ordering for 1-1.5 ns (**b**-**c**), the initially formed bilayer at 3-4 ns (**c**), a metastable pore configuration during 10-20 ns ($\mathbf{c}_{eq}$), and finally the equilibrated defect free bilayer from 25 to 50 ns ($\mathbf{d}_{eq}$).



Supporting figure S3 Disruption of the transmembrane water pore. Headgroup atoms are drawn orange and the lipid tails shown with purple bonds. The water molecules are drawn with dark-blue oxygen and light-blue hydrogen atoms. After 3 ns the initial bilayer has just assembled and the pore is relatively large and unstable. The equilibrium pore shown at 15 ns is smaller but still a serious defect; it is not until 19.7 ns we reach a critical point for the stability of this pore. After 19.9 ns of simulation, the stabilizing headgroups retract to the interface, and 600 ps later there are only small defects remaining. The final equilibrated bilayer structure is reached after 25 ns.